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Diastolic Blood Pressure is a Risk Factor for Peri-procedural Stroke Following Carotid Endarterectomy in Asymptomatic Patients

D.D. de Waard [a,b], G.J. de Borst [b], R. Bulbulia [c], A. Huibers [a,b], A. Halliday [a,*], on behalf of the Asymptomatic Carotid Surgery Trial-1 Collaborative Group

[a] Nuffield Department of Surgical Sciences, University of Oxford, Level 6 John Radcliffe Hospital, Oxford OX3 9DU, UK
[b] Department of Vascular Surgery, University Medical Centre Utrecht, PO Box 85500, Utrecht, The Netherlands
[c] Medical Research Council Population Health Research Unit, Clinical Trial Service Unit & Epidemiological Studies Unit, Nuffield Department of Population Health, Richard Doll Building, Old Road Campus Roosevelt Drive, Oxford OX3 7LF, UK

WHAT THIS PAPER ADDS

The net benefit of carotid revascularisation is highly dependent on procedural risk. In this paper, diastolic blood pressure is shown to be an independent risk factor for peri-procedural stroke/death following carotid endarterectomy (CEA) in the Asymptomatic Carotid Surgery Trial-1. This is in agreement with a recent study in symptomatic patients undergoing CEA. Better blood pressure regulation in the peri-procedural period has the potential to make carotid surgery safer, especially for asymptomatic patients where there is time to treat hypertension pre-operatively.

Objective/Background: Carotid endarterectomy (CEA) prevents future stroke, but this benefit depends on detection and control of high peri-operative risk factors. In symptomatic patients, diastolic hypertension has been causally related to procedural stroke following CEA. The aim was to identify risk factors causing peri-procedural stroke in asymptomatic patients and to relate these to timing of surgery and mechanism of stroke.
Methods: In the first Asymptomatic Carotid Surgery Trial (ACST-1), 3,120 patients with severe asymptomatic carotid stenosis were randomly assigned to CEA plus medical therapy or to medical therapy alone. In 1,425 patients having their allocated surgery, baseline patient characteristics were analysed to identify factors associated with peri-procedural (< 30 days) stroke or death. Multivariate analysis was performed on risk factors with a p value < .3 from univariate analysis. Event timing and mechanism of stroke were analysed using chi-square tests.
Results: A total of 36 strokes (27 ischaemic, four haemorrhagic, five unknown type) and six other deaths occurred during the peri-procedural period, resulting in a stroke/death rate of 2.9% (42/1,425). Diastolic blood pressure at randomisation was the only significant risk factor in univariate analysis (odds ratio [OR] 1.34 per 10 mmHg, 95% confidence interval [CI] 1.04–1.72; $p = .02$) and this remained so in multivariate analysis when corrected for sex, age, lipid lowering therapy, and prior infarcts or symptoms (OR 1.34, 95% CI 1.05–1.72; $p = .02$). In patients with diastolic hypertension (> 90 mmHg) most strokes occurred during the procedure (67% vs. 20%; $p = .02$).
Conclusion: In ACST-1, diastolic blood pressure was the only independent risk factor associated with peri-procedural stroke or death. While the underlying mechanisms of the association between lower diastolic blood pressure and peri-procedural risk remain unclear, good pre-operative control of blood pressure may improve procedural outcome of carotid surgery in asymptomatic patients.

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INTRODUCTION

Large randomised trials in symptomatic and asymptomatic patients have shown that carotid endarterectomy (CEA) prevents stroke.[1,2] The overall benefit depends on interventional hazard and the long-term benefit from stroke risk reduction. To reduce interventional hazard, it is important to understand mechanisms causing peri-procedural stroke and treat factors associated with increased risk.[3] For asymptomatic patients there is usually time for optimisation before intervention, thereby minimising the hazards of surgery.

Haemodynamic instability has been identified previously as a risk factor for surgery, and remains important, even

* Corresponding author. Nuffield Department of Surgical Sciences, University of Oxford, Level 6 John Radcliffe Hospital, Oxford OX3 9DU, UK.
E-mail address: alison.halliday@nds.ox.ac.uk (A. Halliday).
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though blood pressure control has improved.[4–6] Recently, the peri-procedural hazards of poor diastolic blood pressure (DBP) control were highlighted by a substudy from the symptomatic International Carotid Stenting Study, which found DBP to be the single independent risk factor for peri-procedural complications (relative risk 1.30 for each +10 mmHg DBP, 95% confidence interval [CI] 1.02–1.66; $p = .04$) in symptomatic patients.[7]

In this study, using data from the large Asymptomatic Carotid Surgery Trial-1 (ACST-1), the aim was to: (i) identify modifiable risk factors for peri-procedural stroke or death following CEA; and (ii) relate these risk factors to the timing and mechanism of stroke.

METHODS

Patient selection

The ACST-1 protocol has been described previously.[8] The trial included 3,120 patients with unilateral or bilateral carotid stenosis, who were randomised to either immediate CEA with medical therapy or to medical therapy alone. Only patients without ipsilateral neurological symptoms in the past 6 months were entered, and patients randomised to immediate surgery were expected to have their operation as soon as reasonably possible. Choice of surgical and anaesthetic technique was left to the surgeons' discretion. All surgeons' track records for CEA had been approved by the trial Technical Management Committee.

Only patients randomised to immediate intervention and who underwent ipsilateral CEA were included in this post-hoc study.

Outcome events

Patients were assessed by a neurologist following surgery and before discharge. Strokes and deaths within 30 days of CEA were considered to have been caused by or related to the procedure. Two independent members of the endpoint adjudication committee reviewed all events reported to the trial office. Any disagreement was resolved through discussion. Strokes were classified according to type (ischaemic or haemorrhagic), severity (non-disabling, disabling, fatal), laterality (ipsilateral, contralateral, vertebrobasilar), and timing (intra-procedural, day 0 post-procedural, day 1–30).

Classification of stroke mechanism

In a previous study involving patients from ACST-1, the most likely pathophysiological mechanisms for peri-procedural stroke were determined.[9] Ischaemic strokes were classified as follows: (i) carotid-embolic, if there was direct visualisation of an intracranial embolus reported on angiographic brain imaging, or when there was a clear association between onset of symptoms and shunt insertion; (ii) haemodynamic, if there was intra- or post-procedural bradycardia (< 40 beats per minute), asystole, or any hypotension requiring treatment; (iii) thrombosis or occlusion of the carotid artery if a residual stenosis or occlusion of the internal carotid artery (ICA) was found by either imaging or re-exploration, irrespective of the occurrence of an embolic or haemodynamic event; (iv) hyperperfusion, when seizures, a throbbing headache, or neurological deficit occurred in conjunction with intracerebral haemorrhage or cerebral oedema on post-procedural brain imaging; (v) cardio-embolic, if atrial fibrillation was detected on electrocardiography immediately after stroke; (vi) undetermined: (a) probably carotid embolic or haemodynamic, in case the ICA was found to be patent, but there was no radiographic evidence to classify stroke carotid-embolic or haemodynamic; (b) probably carotid-embolic or thrombotic occlusion, when stroke occurred intra-procedurally in the absence of any haemodynamic or cardio-embolic event; (c) all other strokes of undetermined origin.

Statistical analysis

Baseline patient characteristics were collected at time of randomisation and analysed as potential risk factors for the combined outcome of peri-procedural stroke or death. Blood pressure was measured according to local hospital protocol (usually bilateral) and the highest value for systolic blood pressure (SBP) and DBP was used for risk factor analysis. Age, blood pressure, and cholesterol were analysed as continuous variables, while ipsi- and contralateral degree of stenosis were analysed as categorical variables. Patients with missing data were excluded from analysis. Univariate binomial logistic regression analysis was used to calculate odds ratios (OR) with 95% Wald CIs for occurrence of peri-procedural stroke or death. A multivariate logistic regression analysis was performed using variables with a p value $< .30$ in univariate analysis. Chi-square analysis of timing of stroke was performed comparing normotensive and hypertensive patients. Hypertension was defined as a DBP of > 90 mmHg and a SBP > 140 mmHg, according to the National Institute for Health and Care Excellence guidelines.[10] Factors with p values $< .05$ were considered significant for all analyses.

RESULTS

Study population

In 1,560 patients allocated to immediate surgery, CEA was eventually undertaken in 1,425/1,560 (91.3%). Most patients (893/1,425; 62.7%) were operated on within 6 weeks of randomisation, and almost all who eventually had their allocated surgery did so within 1 year (1,388/1,425; 97.4%). Two thirds of participants were men (66.3%) and the mean ± SD age of all patients was 69 ± 7.5 years. Mean ± SD stenosis in the operated carotid artery was 80 ± 11%. The mean ± SD SBP and DBP at randomisation were 154 ± 22 mmHg and 83 ± 11 mmHg, respectively. Baseline patient characteristics and their peri-procedural risk of stroke or death are shown in Table 1.

Outcome events

Peri-procedural stroke or death was uncommon in ACST-1 (42/1,425; 2.9%) and events are shown in Table 2. Most

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